ARTICLE

OBC
www.rsc.org/obc

Meerwein–Ponndorf–Verley alkynylation of aldehydes: Essential modification of aluminium alkoxides for rate acceleration and asymmetric synthesis†

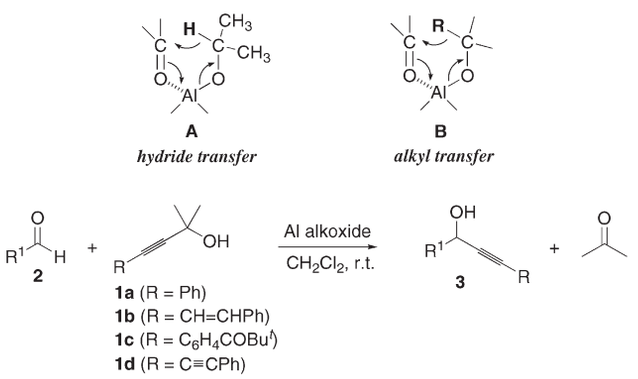
Takashi Ooi, Tomoya Miura, Kohsuke Ohmatsu, Akira Saito and Keiji Maruoka*
Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan. E-mail: maruoka@kuchem.kyoto-u.ac.jp

Received 22nd July 2004, Accepted 15th September 2004
First published as an Advance Article on the web 7th October 2004

A novel carbonyl alkynylation has been accomplished based on utilization of the Meerwein–Ponndorf–Verley (MPV) reaction system. The success of the MPV alkynylation crucially depends on the discovery of the remarkable ligand acceleration effect of 2,2′-biphenol. For example, the alkynylation of chloral (**2c**) with the aluminium alkoxide **6** (R = Ph), prepared *in situ* from Me_3Al, 2,2′-biphenol and 2-methyl-4-phenyl-3-butyn-2-ol (**1a**) as an alkynyl source, proceeded smoothly in CH_2Cl_2 at room temperature to give the desired propargyl alcohol **3ca** in almost quantitative yield after 5 h stirring. The characteristic feature of this new transformation involving no metal alkynides can be visualized by the fact that the alkynyl group bearing keto carbonyl was transferred successfully to aldehyde carbonyl without any side reactions on keto carbonyl. Although the use of (*S*)-1,1′-bi-2-naphthol and its simple analogues was found to be unsuitable for inducing asymmetry in this reaction, design of new chiral biphenols bearing a certain flexibility of the biphenyl axis led to satisfactory results in terms of enantioselectivity as well as reactivity.

Introduction

In 1925 Meerwein[1] and Verley[2] independently reported the reduction of aldehydes with primary alcohols in the presence of aluminium ethoxide, and in the next year Ponndorf[3] extended the scope to the reduction of ketones using secondary alcohols and their aluminium alkoxides, particularly aluminium isopropoxide ($Al(OPr^i)_3$). This type of reaction, *i.e.*, Meerwein–Ponndorf–Verley (MPV) reduction is believed to proceed *via* a six-membered transition state [**A**] and can be performed under mild conditions both in the laboratory and on a large scale without sophisticated experimental technique, generally exhibiting high chemoselectivity (Scheme 1).[4] Accordingly, numerous studies have been carried out to expand the inherent potential of this classical yet important organic transformation as exemplified by the recent elaborations of lanthanides and transition metal catalysts as well as modified aluminium alkoxides.[5,6] During our continuous effort toward the development of new MPV reduction systems, we have been interested for some time in the possibility of alkyl transfer through the MPV process, which should provide a practical, nonorganometallic way for carbonyl alkylation.[7–9] However, developing the MPV alkylation seemed to be a great challenge because of the inertness of alkyl transfer [**B**] compared to the facile hydride transfer [**A**] in the MPV reduction. In pursuing this project, we chose 1,1-dimethyl-3-alkyl-2-propyn-1-ol (**1**) as an alkynyl source in view of the susceptibility of generating the corresponding carbanion through the formation of acetone, and envisioned that employment of appropriate aluminium ligand would lead to stabilization of the desired transition state, facilitating the expected alkynyl transfer. Herein we wish to describe details of the development of the MPV alkynylation of various reactive aldehydes.[10] The reaction was further lifted to the enantioselective stage for the first time by designing a new, axially chiral aluminium alkoxide with conformational flexibility.



Scheme 1

Results and discussion

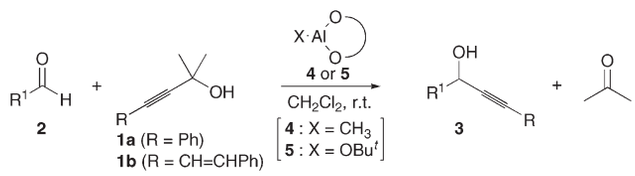
1. Development of the Meerwein–Ponndorf–Verley (MPV) alkynylations

First, we prepared $Al(OC(CH_3)_2C{\equiv}CPh)_3$ as a typical aluminium alkoxide for the MPV alkynylation by treatment of propargylic alcohol **1a** (3 equiv) in CH_2Cl_2 with a 1 M hexane solution of Me_3Al (1 equiv) at room temperature for 30 min, and evaluated its intrinsic reactivity with 2,2-dichlorodecanal (**2a**)[11,12] as a representative substrate (Scheme 2). Upon stirring an equimolar mixture of the aldehyde **2a** and the *in situ* generated $Al(OC(CH_3)_2C{\equiv}CPh)_3$ at room temperature for 5 h, the desired secondary propargyl alcohol **3aa** was obtained in only a trace amount and most of the starting aldehyde was recovered. This result led us to investigate the effect of aluminium ligands on the reaction and several commercially available phenol derivatives were examined. Although the use of $(PhC{\equiv}CC(CH_3)_2O)_2AlOPh$ [derived from **1a** and Me_2AlOPh] brought no appreciable rate acceleration, aluminium alkoxide with two phenoxy ligands, $PhC{\equiv}CC(CH_3)_2OAl(OPh)_2$, on reaction with **2a** under otherwise identical conditions gave **3aa** in higher yield (16%) (Scheme 2). Employment of *o*-phenylenedioxy and *o*,*o*′-biphenylenedioxy ligands further enhanced the rate of alkynylation and **3aa** was obtained in 20% and 53% yields, respectively. Eventually, a synthetically useful level of chemical yield was attained with (*o*,*o*′-biphenylenedioxy)methylaluminium (**4**) in

† Electronic supplementary information (ESI) available: Preparation and spectroscopic characterization of tertiary alkynyl alcohols **1**, aldehydes **2** and chiral ligands **10**. See http://www.rsc.org/suppdata/ob/b4/b411090k/

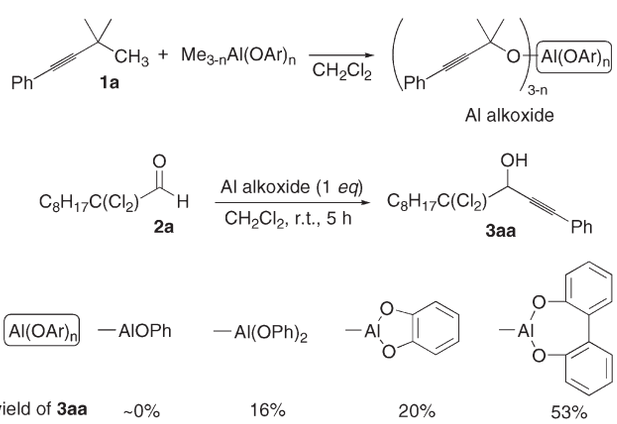
DOI: 10.1039/b411090k

Table 1 MPV alkynylation of various aldehydes[a]



Entry	Aldehyde, **2** R^1	Alkyl source **1** R (equiv)	Al reagent	Reaction time/h	Product **3** (% yield)[b]	Product
1	$CH(Cl)(CH_2)_7CH_3$ (**2b**)	Ph (3)	**4**	2	40 (78 : 32)[c]	**3ba**
2		CH=CHPh (3)	**4**	1	80 (75 : 25)[c]	**3bb**
3		CH=CHPh (3)	**4** (10 mol%)	5	72 (76 : 24)[c]	**3bb**
4	$C(Cl_2)(CH_2)_7CH_3$ (**2a**)	Ph (1)	**4**	5	53	**3aa**
5		Ph (3)	**4**	5	70	**3aa**
6		Ph (3)	**5**	5	61	**3aa**
7		CH=CHPh (1)	**4**	2	42	**3ab**
8		CH=CHPh (3)	**4**	2	66	**3ab**
9	CCl_3 (**2c**)	Ph (1)	**4**	5	81	**3ca**
10		Ph (3)	**4**	5	97	**3ca**
11		Ph (3)	**5**	5	84	**3ca**
12		Ph (3)	**4** (20 mol%)	12	63	**3ca**
13		CH=CHPh (1)	**4**	2	85	**3cb**
14		CH=CHPh (2)	**4**	5	99	**3cb**
15	CBr_3 (**2d**)	Ph (1)	**4**	5	52	**3da**
16		Ph (3)	**4**	5	81	**3da**
17		CH=CHPh (1)	**4**	2.5	58	**3db**
18		CH=CHPh (3)	**4**	2.5	89	**3db**
19	C_6F_5 (**2e**)	Ph (1)	**4**	5	67	**3ea**
20		Ph (3)	**4**	5	85	**3ea**
21		Ph (3)	**5**	5	75	**3ea**
22		Ph (3)	**4** (10 mol%)	12	51	**3ea**
23		CH=CHPh (1)	**4**	1.5	79	**3eb**
24		CH=CHPh (3)	**4**	1.5	99	**3eb**
25	C≡CPh (**2f**)	Ph (5)	**4**[d]	1	54[e]	**3fa**

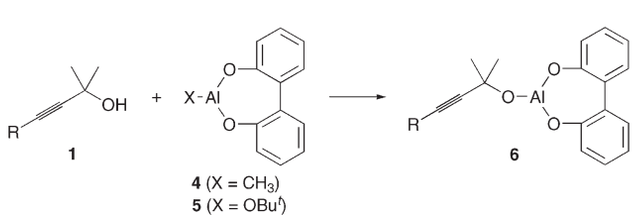
[a] Unless otherwise noted, alcohol **1** was reacted with Al reagent **4** or **5** (1 equiv) in CH_2Cl_2 at room temperature for 10 min, and then treated with aldehyde **2** under the given reaction conditions. [b] Isolated yield. [c] *Erythro*/*threo* ratio of **3** (R = Ph or CH=CHPh) was determined by ^1H NMR analysis. The relative configuration of these isomers was correlated, after hydrogenation to the corresponding saturated chlorohydrins, with that of alkylation products of 2-chlorodecanal by the corresponding Grignard reagents.[19] [d] Use of 5 equiv of Al reagent. [e] The alkynylation product **3fa** (R = Ph, R^1 = PhC≡C) works as a hydride source for the MPV reduction of the starting aldehyde to furnish 1,5-diphenyl-1,4-pentadiyn-3-one (17%) as a side-reaction product.



Scheme 2

the presence of excess propargylic alcohol **1a** (3 equiv) (entry 5 in Table 1).[13]

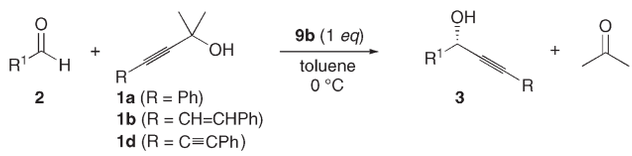
A variety of reactive aldehydes[14] were examined as substrates for this MPV alkynylation system with **1a** and **1b**, and the results are summarized in Table 1. The requisite (propargyloxy)aluminium reagents **6** are also readily accessible from (*o*,*o*′-biphenylenedioxy)(*t*-butoxy)aluminium (**5**) and **1** by the ligand exchange and the effectiveness of the preparative method was also demonstrated (Scheme 3 and entries 6, 11 and 21).[15] The reaction generally requires a stoichiometric amount of aluminium alkoxides, probably because of the difficulty of ligand exchange between the *in situ* formed aluminium alkoxide of the product and the tertiary propargyl alcohol **1**. However, the alkynylation proceeds catalytically in certain cases (entries 3, 12 and 22). Acetylenic aldehyde **2f** can also be transformed to the corresponding secondary propargylic alcohol **3fa** under the MPV alkynylation conditions using **6** (R = Ph), albeit the product can function as a good hydride donor to the starting aldehyde through the MPV process, producing the corresponding ketone and alcohol as side products.[16] Since the MPV reaction is reversible, the overall efficiency is subtly influenced by the steric and electronic properties of the aldehydic substrates **2** and alkynyl donors **1** as well as reaction conditions as shown in Table 1.



Scheme 3

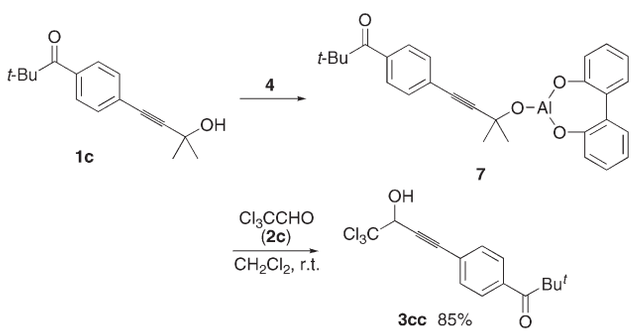
One characteristic feature of the MPV alkynylation is the chemoselective transfer of functionalized alkynyl groups to aldehyde carbonyls. For instance, functionalized aluminium reagent **7** can be readily prepared from the corresponding tertiary alcohol **1c** and **4**, and the subsequent reaction with chloral (**2c**) was found to proceed smoothly at room temperature to furnish alcohol **3cc** in 85% yield without suffering from any undesired reactions on keto carbonyl (Scheme 4).

Table 2 Asymmetric MPV alkynylation of various reactive aldehydes[a]

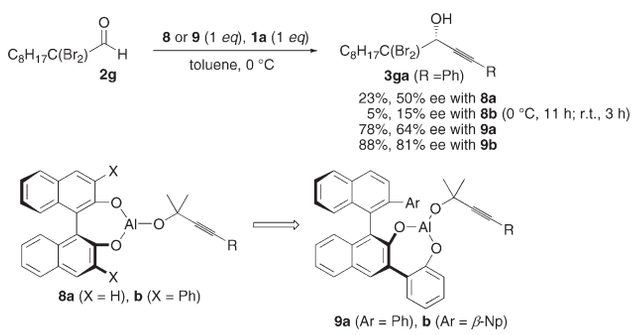


Entry	Aldehyde (R^1)	Alkyl source (R)	Time/h	Yield (%)[b]	ee (%)[c] (config)[d]	Product
1	$C(Br_2)(CH_2)_7CH_3$ (**2g**)	Ph	1.5	78	64[e]	**3ga**
2		Ph	1.5	88	81	**3ga**
3		CH=CHPh	1.5	82	74	**3gb**
4	$C(Br_2)(CH_2)_3CH_3$ (**2h**)	Ph	1	84	78 (*R*)	**3ha**
5		CH=CHPh	1.5	81	80	**3hb**
6	$C(Br_2)CH_2Ph$ (**2i**)	Ph	1	70	82	**3ia**
7		CH=CHPh	5	72	67	**3ib**
8	CCl_3 (**2c**)	Ph	18	85	83 (*R*)	**3ca**
9		CH=CHPh	1.5	99	85	**3cb**
10		C≡CPh	1.5	73	71	**3cd**
11	CBr_3 (**2d**)	Ph	18	87	90 (*R*)	**3da**
12		CH=CHPh	1.5	94	83	**3db**
13		C≡CPh	5	71	86	**3dd**
14	CCl=CHPh (**2j**)	Ph	1.5	30[f,g]	96	**3ja**

[a] Unless otherwise noted, aldehyde **2** was treated with *in situ* generated aluminium alkoxide **9b** (1 equiv) in the presence of **1** (1 equiv) in distilled toluene at 0 °C. [b] Isolated yield. [c] Enantiopurity was determined by HPLC analysis using a following chiral column with hexane/*i*-PrOH as solvent: Daicel Chiralcel OJ for entries 1, 2, 12 and 13; Daicel Chiralcel OD for entries 3, 4, 6, 8, 10 and 11; Daicel Chiralpak AD for entries 5, 7, 9 and 14. [d] Absolute configuration was established, after conversion to the known products, by comparing the optical rotation with the literature values. See the Experimental Section. [e] With aluminium alkoxide **9a**. [f] Use of each 2 equiv of Al reagent and **1**. [g] The alkynylation product **3ja** (R = Ph, R^1 = PhCH=CCl) works as a hydride source for the MPV reduction of the starting aldehyde to furnish 2-chloro-1,5-diphenyl-1-penten-4-yn-3-one and 2-chloro-3-phenyl-2-propen-1-ol as side-reaction products.



Scheme 4



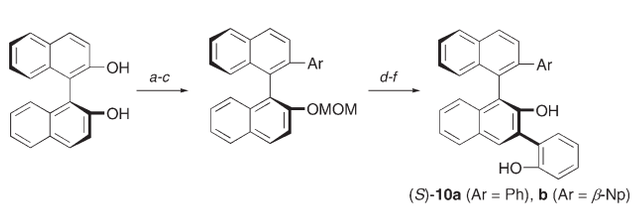
Scheme 5

2. Development of new chiral aluminium alkoxides for the asymmetric Meerwein–Ponndorf–Verley (MPV) alkynylations

In light of the remarkable ligand acceleration effect exerted by *o*,*o*′-biphenyldioxy moiety of **6**, we further envisaged that the employment of chiral C_2-symmetric biphenyl type compounds as an aluminium ligand would lead to the asymmetric version of this unprecedented transformation: this, if successful, could provide a new yet practical method for the asymmetric synthesis of optically active propargylic alcohols,[17,21] versatile and useful chiral building blocks in organic synthesis.

On the basis of this hypothesis, we first used commercially available (*S*)-1,1′-bi-2-naphthol as a chiral ligand and examined the asymmertic Meerwein–Ponndorf–Verley type alkynyl transfer reaction of 2,2-dibromodecanal (**2g**) as a representative system. Thus, the chiral aluminium alkoxide **8a** (R = Ph) was prepared by the simple treatment of (*S*)-1,1′-bi-2-naphthol (1 equiv) with Me_3Al (1 equiv) in toluene at room temperature for 0.5 h and followed by 2-methyl-4-phenyl-3-butyn-2-ol (**1a**, 1 equiv) for an additional 0.5 h. Subsequent reaction with the aldehyde **2g** in the presence of an additional 1 equiv of **1a** at 0 °C for 18 h gave rise to the corresponding secondary propargyl alcohol **3ga** in 23% yield with moderate enantioselectivity (50% ee).[18] Encouraged by the initial result, we attempted the use of (*S*)-3,3′-diphenyl-1,1′-bi-2-naphthol-derived aluminium alkoxide **8b** (R = Ph), which turned out to diminish both reactivity and selectivity (5% yield, 15% ee at 0 °C for 11 h and at room temperature for 3 h) (Scheme 5).

With this information, we assumed that certain flexibility of the biphenyl axis would be prerequisite to attain an ample ligand acceleration effect, and undertook the design of a new, axially chiral aluminium alkoxide **9** (Scheme 5). The requisite optically pure biphenol, (*S*)-**10**, can be readily prepared from (*S*)-1,1′-bi-2-naphthol in six-step sequences as illustrated in Scheme 6. Sequential treatment of (*S*)-**10a** (1 equiv) in toluene with Me_3Al in hexane and **1a** (1 equiv) at room temperature for 1 h generated a conformationally flexible chiral aluminium alkoxide **9a** (R = Ph). This subsequently reacted with 2,2-dibromodecanal (**2g**) in the presence of an additional 1 equiv of **1a** (R = Ph) at 0 °C for 1.5 h to furnish **3ga** in 78% yield, whose enantiomeric excess was determined to be 64% ee as included in Scheme 5 (entry 1 in Table 2).



Scheme 6 (a) Tf_2O, *i*-Pr_2NEt, CH_2Cl_2. (b) MeMgI, then ArMgBr, $NiCl_2$(dppe), ether. (c) NaH, MOMCl, THF. (d) BuLi, THF, then dry Br_2. (e) *o*-MOMO-PhB$(OH)_2$, $Pd(PPh_3)_4$, $Ba(OH)_2{\cdot}8H_2O$, DME, H_2O. (f) conc. HCl, dioxane.

Fortunately, switching the aryl moiety (Ar) to β-naphthyl (**9b**) further increased both the chemical yield and the enantioselectivity (88%, 81% ee) (Scheme 5 and entry 2).

Other selected examples summarized in Table 2 demonstrated the effectiveness of the present system in the asymmetric MPV alkynylation of various reactive aldehydes. It should be particularly emphasized that facile enantioselective transfer of enyne and diyne moieties appeared feasible to produce the corresponding optically active, more conjugated secondary propargylic alcohols (entries 3, 5, 7, 9, 10, 12 and 13), indicating the distinct advantage of this method. Although the highest enantioselectivity was observed in the reaction with α-chlorocinnamaldehyde, the chemical yield was not synthetically satisfactory mainly due to the intervention of the MPV hydride transfer process (entry 14).

Summary

We have successfully developed a MPV alkynylation procedure which is highly effective for the selective alkynylation of aldehydes under mild conditions. The alkynylation can be performed without using alkynyl metal reagents by taking advantage of the ligand-acceleration effect of modified aluminium reagents. The asymmetric version of this reaction has also been achieved by the employment of newly designed axially chiral biphenol ligands bearing conformational flexibility. Thus far, successful MPV alkynylation has been limited to reactive aldehydes. Nevertheless, the present study sheds light on an entirely new aspect of MPV reaction system, which, together with the inherent advantage of MPV reactions, makes it an attractive tool for chemo- and stereoselective carbonyl alkylations.

Experimental

General

Infrared (IR) spectra were recorded on a Shimadzu FT-IR 8200A spectrometer. ^{1}H NMR spectra were measured on a Varian Gemini-300 spectrometer and a JEOL JNM-FX400 spectrometer. Analytical gas–liquid phase chromatography (GLC) was performed on Shimadzu GC-14B instruments equipped with a flame ionization detector and a capillary column of PEG-HT (0.25 × 25 000 mm) using nitrogen as carrier gas. High performance liquid chromatography (HPLC) was done with Shimadzu 10A instruments using 4.6 mm × 25 cm Daicel Chiralcel OD, OJ and Chiralpak AD. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. All experiments were carried out under an atmosphere of dry argon. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel (E. Merck 9385). The high-resolution mass spectra (HRMS) were conducted at the School of Agriculture, Hokkaido University and at the School of Engineering, Kyoto University, and also performed on Applied Biosystems Mariner API-TOF workstation and JEOL JMS-HX100. Microanalyses were accomplished at the School of Pharmaceutical Sciences, Kyoto University.

In experiments requiring dry solvents, ether and tetrahydrofuran (THF) were purchased from Kanto Chemical Co. Inc. as "Dehydrated". Benzene and hexane were dried over sodium metal. *N*,*N*-Dimethylformamide (DMF) was stored over 4 Å molecular sieve pellets. Dichloromethane (CH_2Cl_2) was freshly distilled from calcium hydride, and toluene was freshly distilled from sodium metal. Pyridine and triethylamine (Et_3N) were stored over potassium hydroxide (KOH) pellets. Trimethylaluminium (Me_3Al) was kindly supplied from Toso-Finechem. Co. Ltd., Japan. A stock solution of **5** was prepared by sequential treatment of 2,2′-biphenol with 1 equiv each of Me_3Al and freshly distilled *t*-BuOH in CH_2Cl_2 at room temperature. 2,2-Dihalogenated and 2-halogenated aldehydes were prepared from the corresponding aliphatic aldehydes according to literature procedures.[11,14] Other simple chemicals were purchased and used as such.

General procedure for Meerwein–Ponndorf–Verley (MPV) alkynylation of 2,2-dichlorodecanal (2a) with aluminium alkoxides drived from various ligands

To a degassed solution of a ligand (0.5 mmol) in freshly distilled CH_2Cl_2 (5 mL) was added a 1 M hexane solution of Me_3Al (0.5 mL, 0.5 mmol) dropwise at room temperature and the mixture was stirred for 0.5 h. After the addition of a solution of alkynyl alcohol **1a** (80.1 mg, 0.5 mmol) in freshly distilled CH_2Cl_2 (1 mL), the resulting mixture was stirred for an additional 0.5 h. 2,2-Dichlorodecanal (**2a**; 112.6 mg, 0.5 mmol) was then introduced and the reaction mixture was stirred for 5 h at room temperature. The resulting solution was poured into 1 M HCl and extractive workup was performed with ether. The combined extracts were washed with brine and dried over Na_2SO_4. Removal of volatiles and purification of the residue by column chromatography on silica gel (EtOAc–hexane = 1 : 12 as eluant) gave the corresponding alcohol **3aa**: ^{1}H NMR ($CDCl_3$) δ 7.47–7.50 (2H, m, Ph), 7.30–7.36 (3H, m, Ph), 4.83 (11H, d, J = 8.8 Hz, C*H*OH), 2.77 (1H, dd, J = 8.8, 1.2 Hz, OH), 2.29–2.38 (2H, m, CH_2CCl_2), 1.74 (2H, quint, J = 6.8 Hz, CH_2CCCl_2), 1.20–1.44 (10H, m, $5CH_2$), 0.88 (3H, t, J = 6.8 Hz, CH_3); IR (liquid film) 3423, 2955, 2926, 2855, 2237, 1599, 1491, 1466, 1445, 1379, 1236, 1069, 951, 756, 691 cm^{-1}. Anal. calcd for $C_{18}H_{24}Cl_2O$: C, 66.06; H, 7.39; Cl, 21.66. Found: C, 65.87; H, 7.58; Cl, 21.45.

General procedure for MPV alkynylation of various reactive aldehydes with aluminium alkoxide 6

2,2′-Biphenol (93.1 mg, 0.5 mmol) was placed in a dry two-neck flask with a stirring bar, and freshly distilled CH_2Cl_2 (5 mL) was introduced. After the suspension was carefully degassed, a 1 M hexane solution of Me_3Al (0.5 mL, 0.5 mmol) was added dropwise at room temperature and the mixture was stirred for 0.5 h. The subsequent treatment with a solution of alkynyl alcohol **1** (0.5–1.5 mmol) in freshly distilled CH_2Cl_2 (1.0 mL) was followed by the continuous stirring for 0.5 h to generate **6** [**6** can also be generated by the treatment of a stock solution of **5** with **1** (1 : 1 molar ratio) at room temperature for 0.5 h]. Then, a reactive aldehyde (0.5 mmol) was added and the resulting mixture was stirred for 1–12 h at room temperature. The reaction was quenched with 1 N HCl and extractive workup was performed with ether. The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (CH_2Cl_2–hexane or EtOAc–hexane as eluant) gave the corresponding alkynyl alcohol.

Alkynyl alcohol 3ba

^{1}H NMR ($CDCl_3$) δ 7.43–7.49 (2H, m, Ph, *erythro* and *threo* isomers), 7.29–7.37 (3H, m, Ph, *erythro* and *threo* isomers), 4.75 (0.78H, dd, J = 8.4, 3.6 Hz, C*H*OH, *erythro* isomer), 4.66 (0.22H, dd, J = 6.4, 5.6 Hz, C*H*OH, *threo* isomer), 4.13 (0.78H, ddd, J = 9.6, 4.4, 3.6 Hz, CHCl, *erythro* isomer), 4.07 (0.22H, ddd, J = 9.6, 5.6, 4.0 Hz, CHCl, *threo* isomer), 2.53 (0.78H, d, J = 8.4 Hz, OH, *erythro* isomer), 2.48 (0.22H, d, J = 6.4 Hz, OH, *threo* isomer), 1.74–2.12 (2H, m, CH_2CCl, *erythro* and *threo* isomers), 1.16–1.73 (12H, m, $6CH_2$, *erythro* and *threo* isomers), 0.88 (3H, t, J = 6.8 Hz, CH_3, *erythro* and *threo* isomers); IR (liquid film) 3382, 2928, 2855, 2233, 1599, 1491, 1466, 1443, 1379, 1124, 1032, 756, 691 cm^{-1}. Anal. calcd for $C_{18}H_{25}ClO$: C, 73.83; H, 8.60; Cl, 12.11. Found: C, 73.74; H, 8.77; Cl, 11.65.

Determination of the relative configuration of the product 3ba

The relative configuration of these isomers were correlated, after hydrogenation to the corresponding saturated

chlorohydrins with 10% Pd/C and hydrogen gas in MeOH, with that of alkylation products of **2b** by the corresponding Grignard reagent.[19] 4-Chloro-1-phenyl-3-dodecanol: ^{1}H NMR ($CDCl_3$) δ 7.25–7.34 (2H, m, Ph, *erythro* and *threo* isomers), 7.16–7.25 (3H, m, Ph, *erythro* and *threo* isomers), 3.96–4.05 (0.78H, m, C*H*OH, *erythro* isomer), 3.87–3.94 (0.22H, m, C*H*OH, *threo* isomer), 3.70–3.78 (0.78H, m, CHCl, *erythro* isomer), 3.59–3.66 (0.22H, m, CHCl, *threo* isomer), 2.86–2.96 (0.78H, m, PhCH, *erythro* isomer), 2.78–2.86 (0.22H, m, PhCH, *threo* isomer), 2.61–2.78 (1H, m, PhCH, *erythro* and *threo* isomers), 1.98 (0.78H, d, J = 6.4 Hz, OH, *erythro* isomer), 1.93 (0.22H, d, J = 7.2 Hz, OH, *threo* isomer), 1.75–1.94 (2H, m, CH_2CCl, *erythro* and *threo* isomers), 1.64–1.75 (2H, m, CH_2CPh, *erythro* and *threo* isomers), 1.42–1.62 (2H, m, CH_2CCCl, *erythro* and *threo* isomers), 1.18–1.42 (10H, br s, $5CH_2$, *erythro* and *threo* isomers), 0.88 (3H, t, J = 6.4 Hz, CH_3, *erythro* and *threo* isomers); IR (liquid film) 3412, 3028, 2926, 2855, 1603, 1497, 1454, 1377, 1307, 1047, 748, 700 cm^{-1}. Anal. calcd for $C_{18}H_{29}ClO$: C, 72.82; H, 9.85; Cl, 11.94. Found: C, 73.09; H, 10.09; Cl, 11.69.

Alkynyl alcohol 3bb

^{1}H NMR ($CDCl_3$) δ 7.25–7.42 (5H, m, Ph, *erythro* and *threo* isomers), 7.00 (1H, d, J = 16.5 Hz, PhCH, *erythro* and *threo* isomers), 6.19 (1H, dt, J = 16.5, 2.1 Hz, PhC=CH, *erythro* and *threo* isomers), 4.67–4.75 (0.75H, m, C*H*OH, *erythro* isomer), 4.58–4.65 (0.25H, m, C*H*OH, *threo* isomer), 4.09 (0.75H, ddd, J = 8.7, 4.8, 3.3 Hz, CHCl, *erythro* isomer), 4.03 (0.25H, ddd, J = 9.6, 5.4, 4.2 Hz, CHCl, *threo* isomer), 2.49 (0.75H, d, J = 8.4 Hz, OH, *erythro* isomer), 2.45 (0.25H, d, J = 6.6 Hz, OH, *threo* isomer), 1.74–2.05 (2H, m, CH_2CCl, *erythro* and *threo* isomers), 1.51–1.70 (2H, m, CH_2CCCl, *erythro* and *threo* isomers), 1.18–1.51 (10H, m, $5CH_2$, *erythro* and *threo* isomers), 0.88 (3H, t, J = 6.9 Hz, CH_3, *erythro* and *threo* isomers); IR (liquid film) 3381, 3032, 2953, 2855, 2212, 1465, 1448, 1379, 1155, 1030, 955, 748, 691 cm^{-1}. Anal. calcd for $C_{20}H_{27}ClO$: C, 75.33; H, 8.53; Cl, 11.12. Found: C, 75.27; H, 8.53; Cl, 11.18.

Confirmation of the relative configuration of the product 3bb

The relative configuration of these isomers was determined by the same procedure as described above.[19] 6-Chloro-1-phenyl-5-tetradecanol: ^{1}H NMR ($CDCl_3$) δ 7.22–7.34 (2H, m, Ph, *erythro* and *threo* isomers), 7.14–7.22 (3H, m, Ph, *erythro* and *threo* isomers), 3.95–4.02 (0.75H, m, C*H*OH, *erythro* isomer), 3.85–3.92 (0.25H, m, C*H*OH, *threo* isomer), 3.68–3.76 (0.75H, m, CHCl, *erythro* isomer), 3.56–3.65 (0.25H, m, CHCl, *threo* isomer), 2.63 (2H, t, J = 7.2 Hz, $PhCH_2$, *erythro* and *threo* isomers), 1.90 (0.75H, d, J = 6.8 Hz, OH, *erythro* isomer), 1.83 (0.25H, d, J = 7.6 Hz, OH, *threo* isomer), 1.11–1.83 (20H, m, $10CH_2$, *erythro* and *threo* isomers), 0.88 (3H, t, J = 7.2 Hz, CH_3, *erythro* and *threo* isomers); IR (liquid film) 3429, 3026, 2926, 2856, 2367, 2338, 1719, 1605, 1497, 1454, 1377, 1290, 1070, 746, 698 cm^{-1}. Anal. calcd for $C_{20}H_{33}ClO$: C, 73.93; H, 10.24; Cl, 10.91. Found: C, 74.21; H, 10.17; Cl, 10.68.

Alkynyl alcohol 3ab

^{1}H NMR ($CDCl_3$) δ 7.24–7.43 (5H, m, Ph), 7.04 (1H, d, J = 16.2 Hz, PhCH), 6.20 (1H, dd, J = 16.2, 1.8 Hz, PhC=CH), 4.79 (1H, dd, J = 8.1, 1.8 Hz, C*H*OH), 2.74 (1H, d, J = 8.1 Hz, OH), 2.27–2.35 (2H, m, CH_2CCl_2), 1.72 (2H, quint, J = 7.2 Hz, CH_2CCCl_2), 1.18–1.45 (10H, m, $5CH_2$), 0.89 (3H, d, J = 7.2 Hz, CH_3); IR (liquid film) 3395, 2926, 2856, 2216, 1448, 1377, 1043, 955, 746, 691 cm^{-1}. Anal. calcd for $C_{20}H_{26}Cl_2O$: C, 67.99; H, 7.42; Cl, 20.07. Found: C, 67.88; H, 7.45; Cl, 20.03.

Alkynyl alcohol 3ea

^{1}H NMR ($CDCl_3$) δ 7.39–7.51 (2H, m, Ph), 7.28–7.39 (3H, m, Ph), 5.97 (1H, d, J = 8.0 Hz, C*H*OH), 2.80 (1H, d, J = 8.0 Hz, OH); IR (KBr) 3172, 2242, 1656, 1506, 1290, 1122, 1053, 984, 915, 756, 693 cm^{-1}. Anal. calcd for $C_{15}H_{17}F_5O$: C, 60.41; H, 2.37. Found: C, 60.43; H, 2.58.

Alkynyl alcohol 3eb

^{1}H NMR ($CDCl_3$) δ 7.26–7.40 (5H, m, Ph), 7.00 (1H, d, J = 16.5 Hz, PhCH), 6.16 (1H, dd, J = 16.5, 1.8 Hz, PhC=CH), 5.93 (1H, d, J = 7.5 Hz, C*H*OH), 2.65 (1H, d, J = 7.5 Hz, OH); IR (KBr) 3394, 2212, 1659, 1527, 1506, 1281, 1020, 990, 753, 690 cm^{-1}. Anal. calcd for $C_{17}H_9F_5O$: C, 62.97; H, 2.80. Found: C, 63.16; H, 2.81.

Alkynyl alcohol 3fa[20]

^{1}H NMR ($CDCl_3$) δ 7.45–7.53 (4H, m, Ph), 7.29–7.39 (6H, m, Ph), 5.59 (1H, d, J = 7.6 Hz, C*H*OH), 2.41 (1H, d, J = 7.6 Hz, OH); IR (liquid film) 3298, 3229, 2232, 1597, 1489, 1443, 1300, 1032, 1015, 995, 914, 754, 689 cm^{-1}.

MPV alkynylation of chloral with aluminium alkoxide 7

To a degassed solution of 2,2′-biphenol (93.1 mg, 0.5 mmol) in freshly distilled CH_2Cl_2 (5 mL) was added a 1 M hexane solution of Me_3Al (0.5 mL, 0.5 mmol) dropwise at room temperature and the mixture was stirred for 0.5 h. A solution of alkynyl alcohol **1c** (244.3 mg, 1 mmol) in freshly distilled CH_2Cl_2 (1 mL) was added to the reaction mixture, and the stirring was continued for an additional 0.5 h. Freshly distilled chloral (73.7 mg, 0.5 mmol) was added to the solution, and the resulting mixture was stirred for 8 h at room temperature. The reaction solution was poured into 1 N HCl and extracted with ether. The ethereal extracts were washed with brine and dried over Na_2SO_4. Removal of volatiles and purification of the residual oil by column chromatography on silica gel (CH_2Cl_2–hexane = 6 : 1 as eluant) gave the desired alkynyl alcohol **3cc** (143.5 mg, 0.43 mmol, 85%): ^{1}H NMR ($CDCl_3$) δ 7.66 (2H, m, Ph), 7.52 (2H, m, Ph), 5.06 (1H, d, J = 9.0 Hz, C*H*OH), 3.31 (1H, br d, J = 9.0 Hz, OH), 1.34 (9H, s, *t*-Bu); IR (liquid film) 3302, 2972, 2367, 2242, 1674, 1603, 1477, 1396, 1367, 1279, 1194, 1175, 1082, 964, 827, 768, 746 cm^{-1}. Anal. calcd for $C_{15}H_{15}Cl_3O_2$: C, 54.00; H, 4.53; Cl, 31.88. Found: C, 54.09; H, 4.69; Cl, 31.60.

Enantioselective MPV alkynylation of 2,2-dibromodecanal (2g) with various chiral aluminium alkoxides

To a carefully degassed solution of a chiral binaphthyl ligand (0.3 mmol) in freshly distilled toluene (3 mL) was added a 1 M hexane solution of Me_3Al (0.3 mL, 0.3 mmol) dropwise at room temperature and the mixture was stirred for 0.5 h. A solution of 2-methyl-4-phenyl-3-butyn-2-ol (**1a**; 96.1 mg, 0.6 mmol) in freshly distilled toluene (1 mL) was introduced and the resulting mixture was stirred for an additional 0.5 h. Then, a solution of 2,2-dibromodecanal (**2g**; 94.2 mg, 0.3 mmol) in distilled toluene (0.5 mL) was carefully added at 0 °C and the reaction mixture was stirred for 1–18 h at 0 °C. The reaction was quenched with 1 M HCl and extracted with ether. The ethereal extracts were washed with brine, dried over Na_2SO_4 and concentrated. The residual oil was purified by column chromatography on silica gel (CH_2Cl_2–hexane or EtOAc–hexane as eluant) to afford the desired alkynyl alcohol **3ga** in an enantioselective manner. Enantiomeric excess was determined by chiral HPLC analysis.

Alkynyl alcohol 3ga

^{1}H NMR ($CDCl_3$) δ 7.46–7.51 (2H, m, Ph), 7.29–7.40 (3H, m, Ph), 4.77 (1H, d, J = 8.8 Hz, C*H*OH), 2.86 (1H, d, J = 8.8 Hz, OH), 2.41–2.56 (2H, m, CH_2CBr_2), 1.77 (2H, quint, J = 7.2 Hz, CH_2CCBr_2), 1.18–1.47 (10H, m, $5CH_2$), 0.88 (3H, t, J = 7.2 Hz, CH_3); IR (liquid film) 3537, 3423, 2926, 2855, 2233, 1491, 1466, 1443, 1379, 1296, 1234, 1057, 756, 691 cm^{-1}. Anal. calcd for $C_{18}H_{24}Br_2O$: C, 51.95; H, 5.81; Br, 38.40. Found: C, 52.19; H, 5.93; Br, 38.46. HPLC (Daicel Chiralcel OJ, hexane–*i*-PrOH = 10 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm)

t_r = 12.2 min (major) and 14.5 min (minor); $[\alpha]_D^{28}$ +6.61° (*c* 1.06, $CHCl_3$); 81% ee.

General procedure for asymmetric MPV alkynylation of various reactive aldehydes with aluminium alkoxide 9b

Chiral ligand (*S*)-**10b** (146.6 mg, 0.3 mmol) was placed in a dry two-neck flask with a stirring bar, and freshly distilled toluene (3 mL) was introduced. After the suspension was carefully degassed, a 1 M hexane solution of Me_3Al (0.3 mL, 0.3 mmol) was added dropwise at room temperature and the mixture was stirred for 0.5 h. After the subsequent treatment with a solution of alkynyl alcohol **1** (0.6 mmol) in freshly distilled toluene (1 mL), the stirring was continued for an additional 0.5 h. Then, a toluene (0.5 mL) solution of freshly distilled aldehyde (0.3 mmol) was added slowly at 0 °C and the resulting mixture was maintained at 0 °C for 1–18 h with stirring. The reaction was quenched with 1 M HCl and extracted with ether. The ethereal extracts were washed with brine and dried over Na_2SO_4. Removal of solvents and purification of the residue by column chromatography on silica gel (CH_2Cl_2–hexane or EtOAc–hexane as eluant) gave the corresponding alkynyl alcohol. Enantiomeric excess was determined by chiral HPLC analysis (Daicel Chiralpak AD, Chiralcel OD and OJ as chiral columns).

Alkynyl alcohol 3gb

^{1}H NMR ($CDCl_3$) δ 7.25–7.42 (5H, m, Ph), 7.04 (1H, d, *J* = 16.4 Hz, PhCH), 6.19 (1H, dd, *J* = 16.4, 2.0 Hz, PhC=CH), 4.73 (1H, dd, *J* = 8.4, 2.0 Hz, C*H*OH), 2.81 (1H, d, *J* = 8.4 Hz, OH), 2.40–2.51 (2H, m, CH_2CBr_2), 1.76 (2H, quint, *J* = 7.2 Hz, CH_2CCBr_2), 1.20–1.42 (10H, m, $5CH_2$), 0.89 (3H, t, *J* = 6.8 Hz, CH_3); IR (liquid film) 3533, 3423, 3030, 2928, 2855, 2214, 1491, 1466, 1448, 1377, 1298, 1038, 955, 748, 691 cm^{-1}. Anal. calcd for $C_{20}H_{26}Br_2O$: C, 54.32; H, 5.93; Br, 36.14. Found: C, 54.25; H, 5.87; Br, 35.47. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 4 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 12.4 min (minor) and 16.0 min (major); $[\alpha]_D^{26}$ +23.93° (*c* 0.91, $CHCl_3$); 74% ee.

Alkynyl alcohol 3ha

^{1}H NMR ($CDCl_3$) δ 7.46–7.52 (2H, m, Ph), 7.30–7.40 (3H, m, Ph), 4.77 (1H, d, *J* = 8.4 Hz, C*H*OH), 2.88 (1H, d, *J* = 8.4 Hz, OH), 2.42–2.55 (2H, m, CH_2CBr_2), 1.76 (2H, quint, *J* = 7.2 Hz, CH_2CCBr_2), 1.44 (2H, sext, *J* = 7.2 Hz, CH_2CCCBr_2), 0.98 (3H, t, *J* = 7.2 Hz, CH_3); IR (liquid film) 3535, 3429, 2959, 2872, 2233, 1599, 1491, 1466, 1443, 1381, 1288, 1234, 1047, 945, 918, 808, 756, 691 cm^{-1}. Anal. calcd for $C_{14}H_{16}Br_2O$: C, 46.70; H, 4.48; Br, 44.38. Found: C, 46.91; H, 4.53; Br, 44.23. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 10 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 15.9 min (*R*) and 17.8 min (*S*); $[\alpha]_D^{30}$ +6.77° (*c* 1.00, $CHCl_3$); 78% ee (*R*).

Assignment of the absolute configuration of 3ha

The absolute configuration of **3ha** was determined, after the reductive debromination of the trimethylsilyl ether of **3ha** with Bu_3SnH in the presence of Et_3B and the successive deprotection with diluted HCl, by comparison with the optical rotation of the known (*S*)-1-phenyl-1-octyn-3-ol.[21] To a solution of **3ha** (90.7 mg, 0.252 mmol, 78% ee), imidazole (25.7 mg, 0.378 mmol) and 4-(dimethylamino)pyridine (3.1 mg, 0.025 mmol) in DMF (1 mL) was added chlorotrimethylsilane (48 µL, 0.378 mmol) at 0 °C, and the resulting mixture was stirred for 5 h at room temperature. The solution was poured into saturated $NaHCO_3$ and extracted with ether. The organic extracts were washed with brine and dried over Na_2SO_4. Evaporation of solvents and purification by column chromatography on silica gel (ether–hexane = 1 : 50 as eluant) gave the silyl ether of **3ha** (102.4 mg, 0.237 mmol, 94%): ^{1}H NMR ($CDCl_3$) δ 7.44–7.49 (2H, m, Ph), 7.29–7.37 (3H, m, Ph), 4.90 (1H, s, CHOSi), 2.35–2.48 (2H, m, CH_2CBr_2), 1.67–1.84 (2H, m, CH_2CCBr_2), 1.43 (2H, sext, *J* = 7.6 Hz, CH_2CCCBr_2), 0.98 (3H, t, *J* = 7.6 Hz, CH_3), 0.28 (9H, s, $(CH_3)_3Si$).

To a solution of the silyl ether (102.4 mg, 0.237 mmol) and Bu_3SnH (128 µL, 0.474 mmol) in toluene (2 mL) was added a 1 M hexane solution of Et_3B (240 µL, 0.237 mmol) at −78 °C and the mixture was stirred for 2 h at the same temperature. The solution was poured into a mixture of 1 M HCl (2 mL) and THF (2 mL), and the resulting mixture was stirred for 1 h at room temperature. After extractive workup with ether, the combined extracts were washed with saturated $NaHCO_3$ and dried over Na_2SO_4. Removal of solvents and purification by column chromatography on silica gel (ether–hexane = 1 : 5 as eluant) afforded 1-phenyl-1-octyn-3-ol (40.3 mg, 0.199 mmol, 84%, 78% ee (*S*)): ^{1}H NMR ($CDCl_3$) δ 7.39–7.47 (2H, m, Ph), 7.28–7.34 (3H, m, Ph), 4.60 (1H, q, *J* = 6.4 Hz, C*H*OH), 1.83 (1H, d, *J* = 6.4 Hz, OH), 1.72–1.86 (2H, m, CH_2COH), 1.46–1.61 (2H, m, CH_2CCOH), 1.29–1.42 (4H, m, $2CH_2$), 0.91 (3H, t, *J* = 6.8 Hz, CH_3); IR (liquid film) 3333, 2955, 2932, 2860, 2361, 1599, 1491, 1466, 1443, 1379, 1339, 1123, 1030, 914, 756, 691 cm^{-1}. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 9 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 12.6 min (*R*) and 31.5 min (*S*); $[\alpha]_D^{21}$ +4.46° (*c* 1.02, $CHCl_3$); 78% ee (*S*).

Alkynyl alcohol 3hb

^{1}H NMR ($CDCl_3$) δ 7.29–7.42 (5H, m, Ph), 7.04 (1H, d, *J* = 16.4 Hz, PhCH), 6.19 (1H, dd, *J* = 16.4, 2.0 Hz, PhC=CH), 4.73 (1H, dd, *J* = 8.4, 2.0 Hz, C*H*OH), 2.83 (1H, d, *J* = 8.4 Hz, OH), 2.39–2.52 (2H, m, CH_2CBr_2), 1.75 (2H, quint, *J* = 7.2 Hz, CH_2CCBr_2), 1.44 (2H, sext, *J* = 7.2 Hz, CH_2CCCBr_2), 0.98 (3H, t, *J* = 7.2 Hz, CH_3); IR (liquid film) 3528, 3398, 3030, 2957, 2932, 2872, 2212, 1448, 1379, 1298, 1211, 1119, 1038, 955, 748, 691 cm^{-1}. Anal. calcd for $C_{16}H_{18}Br_2O$: C, 49.77; H, 4.70; Br, 41.39. Found: C, 49.79; H, 4.65; Br, 41.52. HPLC (Daicel Chiralpak AD, hexane–*i*-PrOH = 9 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 21.6 min (major) and 26.1 min (minor); $[\alpha]_D^{27}$ +8.04° (*c* 0.99, $CHCl_3$); 80% ee.

Alkynyl alcohol 3ia

^{1}H NMR ($CDCl_3$) δ 7.47–7.54 (4H, m, Ph), 7.31–7.40 (6H, m, Ph), 4.63 (1H, d, *J* = 9.2 Hz, C*H*OH), 3.97 (1H, d, *J* = 14.0 Hz, PhCH), 3.87 (1H, d, *J* = 14.0 Hz, PhCH), 2.89 (1H, d, *J* = 9.2 Hz, OH); IR (liquid film) 3530, 3445, 3063, 3032, 2928, 2232, 1599, 1491, 1454, 1427, 1377, 1298, 1234, 1078, 1051, 955, 756, 700, 691 cm^{-1}. MS (ESI) *m*/*z* 431, 429 (100%), 427 ([M + Cl]$^-$). HRMS (ESI-TOF) calcd for $C_{17}H_{14}ClBr_2O$: 426.9094 ([M + Cl]$^-$). Found: 426.9091 ([M + Cl]$^-$). HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 20 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 26.5 min (minor) and 34.2 min (major); $[\alpha]_D^{27}$ +46.18° (*c* 1.00, $CHCl_3$); 82% ee.

Alkynyl alcohol 3ib

^{1}H NMR ($CDCl_3$) δ 7.27–7.48 (10H, m, Ph), 7.05 (1H, d, *J* = 16.0 Hz, PhCH=C), 6.21 (1H, dd, *J* = 16.0, 1.6 Hz, PhC=CH), 4.69 (1H, dd, *J* = 8.8, 1.6 Hz, C*H*OH), 3.71 (1H, d, *J* = 14.4 Hz, PhCH), 3.64 (1H, d, *J* = 14.4 Hz, PhCH), 2.75 (1H, d, *J* = 8.8 Hz, OH); IR (liquid film) 3533, 3433, 3061, 3032, 2928, 2212, 1603, 1495, 1454, 1427, 1375, 1296, 1265, 1234, 1211, 1157, 1067, 1032, 957, 748, 700 cm^{-1}. Anal. calcd for $C_{19}H_{16}Br_2O$: C, 54.32; H, 3.84; Br, 38.04. Found: C, 54.05; H, 3.95; Br, 38.00. HPLC (Daicel Chiralpak AD, hexane–*i*-PrOH = 2 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 12.9 min (minor) and 15.0 min (major); $[\alpha]_D^{26}$ +51.11° (*c* 1.16, $CHCl_3$); 67% ee.

Alkynyl alcohol 3ca[22]

^{1}H NMR ($CDCl_3$) δ 7.47–7.54 (2H, m, Ph), 7.31–7.43 (3H, m, Ph), 5.04 (1H, d, *J* = 9.3 Hz, C*H*OH), 3.11 (1H, d, *J* = 9.3 Hz, OH); IR (liquid film) 3542, 3393, 3082, 2362, 2243, 1599, 1491,

1445, 1385, 1298, 1072, 1043, 937, 824, 756, 727, 691 cm^{-1}. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 30 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 44.9 min (*S*) and 52.1 min (*R*); $[\alpha]_D^{26}$ −2.50° (*c* 1.13, $CHCl_3$); 83% ee (*R*).

Determination of the absolute configuration of 3ca

The absolute configuration of **3ca** was determined, after hydrogenation of the triple bond with 10% Pd/C under hydrogen gas in MeOH, by comparison with the optical rotation of the known (*R*)-4-phenyl-1,1,1-trichloro-2-butanol:[23] ^{1}H NMR ($CDCl_3$) δ 7.18–7.38 (5H, m, Ph), 3.99 (1H, ddd, *J* = 10.0, 5.2, 2.0 Hz, C*H*OH), 3.00 (1H, ddd, *J* = 13.6, 9.2, 4.8 Hz, PhCH), 2.73–2.83 (2H, m, PhCH and OH), 2.33–2.44 (1H, m, PhCCH), 1.93–2.06 (1H, m, PhCCH); IR (liquid film) 3558, 2964, 2939, 1601, 1497, 1456, 1244, 1096, 1070, 1053, 997, 812, 785, 754, 702 cm^{-1}. HPLC (Daicel Chiralpak AD, hexane–*i*-PrOH = 30 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 19.6 min (*S*) and 21.6 min (*R*); $[\alpha]_D^{27}$ +42.13° (*c* 1.00, $CHCl_3$); 83% ee (*R*).

Alkynyl alcohol 3cb

^{1}H NMR ($CDCl_3$) δ 7.25–7.50 (5H, m, Ph), 7.08 (1H, d, *J* = 16.5 Hz, PhCH), 6.19 (1H, dd, *J* = 16.5, 1.8 Hz, PhC=CH), 5.00 (1H, d, *J* = 8.7 Hz, C*H*OH), 3.08 (1H, d, *J* = 8.7 Hz, OH); IR (KBr) 3482, 3022, 2922, 2220, 1489, 1447, 1396, 1292, 1259, 1211, 1165, 1055, 957, 827, 779, 746, 689 cm^{-1}. Anal. calcd for $C_{12}H_9Cl_3O$: C, 52.30; H, 3.29; Cl, 38.60. Found: C, 52.55; H, 3.41; Cl, 38.72. HPLC (Daicel Chiralpak AD, hexane–*i*-PrOH = 20 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 46.7 min (minor) and 54.8 min (major); $[\alpha]_D^{26}$ +1.09° (*c* 1.00, $CHCl_3$); 85% ee.

Alkynyl alcohol 3cd

^{1}H NMR ($CDCl_3$) δ 7.48–7.56 (2H, m, Ph), 7.30–7.43 (3H, m, Ph), 4.96 (1H, d, *J* = 9.2 Hz, C*H*OH), 3.16 (1H, d, *J* = 9.2 Hz, OH); IR (KBr) 3522, 2936, 2359, 2341, 2243, 1489, 1441, 1379, 1317, 1256, 1117, 1057, 1027, 860, 829, 795, 756, 687 cm^{-1}. MS (ESI) *m*/*z* 311, 309 (100%), 307 ([M + Cl]$^-$), 237, 235. HRMS (ESI-TOF) calcd for $C_{12}H_7Cl_4O$: 306.9246 ([M + Cl]$^-$). Found: 306.9237 ([M + Cl]$^-$). HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 4 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 16.4 min (minor) and 23.9 min (major); $[\alpha]_D^{27}$ −0.72° (*c* 1.00, $CHCl_3$); 71% ee.

Alkynyl alcohol 3da

^{1}H NMR ($CDCl_3$) δ 7.50–7.54 (2H, m, Ph), 7.32–7.43 (3H, m, Ph), 5.02 (1H, d, *J* = 9.0 Hz, C*H*OH), 3.26 (1H, d, *J* = 9.0 Hz, OH); IR (liquid film) 3503, 3443, 2361, 2237, 1489, 1443, 1387, 1293, 1225, 1069, 1028, 920, 779, 756, 691 cm^{-1}. Anal. calcd for $C_{10}H_7Br_3O$: C, 31.37; H, 1.84; Br, 62.61. Found: C, 31.38; H, 1.94; Br, 62.29. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 10 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 24.5 min (*R*) and 29.2 min (*S*); $[\alpha]_D^{26}$ −3.69° (*c* 1.10, $CHCl_3$); 90% ee (*R*).

Determination of the absolute configuration of 3da

The absolute configuration of **3da** was determined, after reductive debromination according to the same procedure as described in the case of **3ha**, by comparison with the optical rotation of the known (*S*)-4-phenyl-3-butyn-2-ol:[24] ^{1}H NMR ($CDCl_3$) δ 7.38–7.45 (2H, m, Ph), 7.27–7.34 (3H, m, Ph), 4.76 (1H, dq, *J* = 6.4, 5.6 Hz, C*H*OH), 1.87 (1H, d, *J* = 5.6 Hz, OH), 1.56 (3H, d, *J* = 6.4 Hz, CH_3); IR (liquid film) 3335, 2982, 2932, 2361, 1599, 1491, 1443, 1371, 1331, 1278, 1107, 1072, 1038, 934, 853, 756, 691 cm^{-1}. HPLC (Daicel Chiralcel OD, hexane–*i*-PrOH = 10 : 1, flow rate = 1.0 mL min^{-1}, λ = 254 nm) t_r = 8.3 min (*R*) and 18.9 min (*S*); $[\alpha]_D^{25}$ −28.36° (*c* 0.65, $CHCl_3$); 90% ee (*S*).

Alkynyl alcohol 3db

^{1}H NMR ($CDCl_3$) δ 7.30–7.45 (5H, m, Ph), 7.09 (1H, d, *J* = 16.2 Hz, PhCH), 6.19 (1H, dd, *J* = 16.2, 1.8 Hz, PhC=CH), 4.98 (1H, dd, *J* = 8.7, 1.8 Hz, C*H*OH), 3.24 (1H, d, *J* = 8.7 Hz, OH); IR (KBr) 3401, 2218, 1489, 1447, 1385, 1274, 1211, 1163, 1072, 1040, 955, 754, 723, 692 cm^{-1}. MS (EI) *m*/*z* 410, 408, 406 (M$^+$), 158, 157 (100%), 152, 141, 139, 129, 128, 127, 115, 70. HRMS (EI) calcd for $C_{12}H_9Br_3O$: 405.8203 (M$^+$). Found: 405.8231 (M$^+$). HPLC (Daicel Chiralcel OJ, hexane–*i*-PrOH = 4 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 30.0 min (minor) and 37.0 min (major); $[\alpha]_D^{26}$ −2.72° (*c* 1.00, $CHCl_3$); 83% ee.

Alkynyl alcohol 3dd

^{1}H NMR ($CDCl_3$) δ 7.50–7.55 (2H, m, Ph), 7.30–7.44 (3H, m, Ph), 4.97 (1H, d, *J* = 9.2 Hz, C*H*OH), 3.27 (1H, d, *J* = 9.2 Hz, OH); IR ($CHCl_3$) 3522, 3298, 2243, 1489, 1441, 1408, 1379, 1317, 1267, 1113, 1047, 754, 689, 660 cm^{-1}. MS (ESI) *m*/*z* 445, 443, 441 (100%), 439 ([M + Cl]$^-$). HRMS (ESI-TOF) calcd for $C_{12}H_7ClBr_3O$: 438.7730 ([M + Cl]$^-$). Found: 438.7727 ([M + Cl]$^-$). HPLC (Daicel Chiralcel OJ, hexane–*i*-PrOH = 4 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 25.0 min (minor) and 30.7 min (major); $[\alpha]_D^{30}$ −2.06° (*c* 1.00, $CHCl_3$); 86% ee.

Alkynyl alcohol 3ja

^{1}H NMR ($CDCl_3$) δ 7.66–7.71 (2H, m, Ph), 7.46–7.53 (2H, m, Ph), 7.29–7.42 (6H, m, Ph), 7.05 (1H, s, PhCH), 5.30 (1H, d, *J* = 7.6 Hz, C*H*OH), 2.59 (1H, d, *J* = 7.6 Hz, OH); IR (KBr) 3504, 3053, 2230, 1638, 1597, 1491, 1448, 1389, 1296, 1223, 1096, 1072, 1018, 964, 926, 880, 754, 691, 650 cm^{-1}. Anal. calcd for $C_{17}H_{13}ClO$: C, 75.98; H, 4.88; Cl, 13.19. Found: C, 75.96; H, 4.81; Cl, 13.11. HPLC (Daicel Chiralpak AD, hexane–*i*-PrOH = 10 : 1, flow rate = 0.5 mL min^{-1}, λ = 254 nm) t_r = 30.0 min (minor) and 37.1 min (major); $[\alpha]_D^{21}$ −12.78° (*c* 0.32, $CHCl_3$); 96% ee.

Acknowledgements

This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan. T.M. is grateful to the Japan Society for the Promotion of Science for Young Scientists for a research fellowship.

References

1 H. Meerwein and R. Schmidt, *Liebigs Ann. Chem.*, 1925, **444**, 221.
2 A. Verley, *Bull. Soc. Chim. Fr.*, 1925, **37**, 537.
3 W. Ponndorf, *Angew. Chem.*, 1926, **39**, 138.
4 Reviews: A. L. Wilds, *Org. React.*, 1944, **2**, 178; R. M. Kellogg, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, I. Fleming, Pergamon Press, Oxford, 1991, vol. 8, p. 88.
5 C. F. de Graauw, J. A. Peters, H. van Bekkum and J. Huskens, *Synthesis*, 1994, 1007; T. Ooi, T. Miura, Y. Itagaki, H. Ichikawa and K. Maruoka, *Synthesis*, 2002, 279 and references cited therein.
6 For recent contributions, see: I. Simpura and V. Nevalainen, *Tetrahedron*, 2001, **57**, 9867; T. Ooi, H. Ichikawa and K. Maruoka, *Angew. Chem., Int. Ed. Engl.*, 2001, **40**, 3610; E. J. Campbell, H. Zhou and S. T. Nguyen, *Angew. Chem., Int. Ed. Engl.*, 2002, **41**, 1020.
7 For MPV type cyanide transfer, see: A. Mori, K. Kinoshita, M. Osaka and S. Inoue, *Chem. Lett.*, 1990, 1171.
8 For the formal analogues to MPV type allylation, see: J. Nokami, K. Yoshizane, H. Matsuura and S.-I. Sumida, *J. Am. Chem. Soc.*, 1998, **120**, 6609; S.-I. Sumida, M. Ohga, J. Mitani and J. Nokami, *J. Am. Chem. Soc.*, 2000, **122**, 1310.
9 For the formally analogous aldol-transfer reaction, see: I. Simpura and V. Nevalainen, *Angew. Chem., Int. Ed. Engl.*, 2000, **39**, 3422.
10 A preliminary communication of this work has been published: T. Ooi, T. Miura and K. Maruoka, *J. Am. Chem. Soc.*, 1998, **120**, 10790. For related studies, see: T. Ooi, K. Takaya, T. Miura and K. Maruoka, *Synlett*, 2000, 69; T. Ooi, K. Takaya, T. Miura, H. Ichikawa and K. Maruoka, *Synlett*, 2000, 1133; T. Ooi, T. Miura, K. Takaya, H. Ichikawa and K. Maruoka, *Tetrahedron*, 2001, **57**, 867.
11 For preparation of 2,2-dihaloaldehydes: R. Verhé, N. D. Kimpe, L. D. Buyck and N. Schamp, *Synthesis*, 1975, 455.

12 We chose 2,2-dihaloaldehydes as representative reactive aldehydes because of the ease of further manipulation of the alkylation products by simple dehalogenation. For the C–Cl bond cleavage, see: S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, 1980, **45**, 849; A. R. Pinder, *Synthesis*, 1980, 425; R. Noyori and Y. Hayakawa, *Org. React.*, 1983, **29**, 163.
13 Attempted allylation of aldehyde **2a** with 2-methyl-4-penten-2-ol and **4** under otherwise similar reaction conditions gave none of the desired homoallylic alcohols, hence excluding the possibility of the stabilized carbocation mechanism in our system, see ref. 8.
14 For preparation of 2-haloaldehydes: L. Blanko, P. Amice and M. Conia, *Synthesis*, 1976, 194.
15 The feebly Lewis acidic **5** can be stored under argon atmosphere and would be advantageous for the preparation of **6** possessing labile functionalities.
16 α,β-Acetylenic aldehydes can be synthesized from terminal alkynes with high efficiency. M. Journet, D. Cai, L. M. DiMichele and R. D. Larsen, *Tetrahedron Lett.*, 1998, **39**, 6427.
17 For recent impressive studies on the enantioselective addition of metalated acetylenes to aldehydes, see: Z. Li, V. Upadhyay, A. E. DeCamp, L. DiMichele and P. J. Reider, *Synthesis*, 1999, 1453; D. E. Frantz, R. Fässler and E. M. Carreira, *J. Am. Chem. Soc.*, 2000, **122**, 1806; N. K. Anand and E. M. Carreira, *J. Am. Chem. Soc.*, 2001, **123**, 9687; D. Moore, W.-S. Huang, M.-H. Xu and L. Pu, *Tetrahedron Lett.*, 2002, **43**, 8831; A. L. Braga, H. R. Appelt, C. C. Silveira, L. A. Wessjohann and P. H. Schneider, *Tetrahedron*, 2002, **58**, 10413; X. Li, G. Lu, W. H. Kwok and A. S. C. Chan, *J. Am. Chem. Soc.*, 2002, **124**, 12636; and references cited therein. See also: P. G. Cozzi, *Angew. Chem., Int. Ed. Engl.*, 2003, **42**, 2895; G. Lu, X. Li, X. Jia, W. L. Chan and A. S. C. Chan, *Angew. Chem., Int. Ed. Engl.*, 2003, **42**, 5057.
18 The use of CH_2Cl_2 as solvent generally provided improved chemical yield but with substantial decrease of the enantiomeric excess in the asymmetric reaction.
19 J. D. Morrison and H. S. Mosher, *Asymmetric Organic Reactions*, American Chemical Society, Washington DC, USA, 1976, p 99.
20 H. Hauptmann and M. Mader, *Synthesis*, 1978, 307.
21 E. J. Corey and K. A. Cimprich, *J. Am. Chem. Soc.*, 1994, **116**, 3151.
22 A. von Roedig, V. Kimmel, W. Lippert and B. Heinrich, *Liebigs Ann. Chem.*, 1972, **755**, 455.
23 E. J. Corey and J. O. Link, *J. Am. Chem. Soc.*, 1992, **114**, 1906.
24 C. J. Helal, P. A. Magriotis and E. J. Corey, *J. Am. Chem. Soc.*, 1996, **118**, 10938.